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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/754,437	01/09/2004	Bonita J.M. Ferrie	MMI1130-1	8712
28213	7590	06/29/2006	EXAMINER	
DLA PIPER RUDNICK GRAY CARY US, LLP 4365 EXECUTIVE DRIVE SUITE 1100 SAN DIEGO, CA 92121-2133			GOLDBERG, JEANINE ANNE	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/754,437	Applicant(s) FERRIE ET AL.	
	Examiner Jeanine A. Goldberg	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/26/06; 4/12/06.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-9,12,13,23,25,26,36,38,48,80 and 81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-9,12,13,23,25,26,36,38,48,80 and 81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 25, 2006 and April 12, 2006 has been entered.
2. This action is in response to the papers filed January 25, 2006 and April 12, 2006. Currently, claims 1, 3-9, 12-13, 23, 25-26, 36, 38, 48, 80-81 are pending.
3. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.
4. Any objections and rejections not reiterated below are hereby withdrawn.
 - a. The Written Description rejection has been withdrawn in view of the amendments to the claims to require SEQ ID NO: 22 and 23 and the presence of the "entire" dog genome sequence.

Maintained Rejections

Priority

5. This application claims priority to provisional application 60/439,188, filed January 10, 2003.

Drawings

6. The drawings are acceptable.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-9, 12-13, 23, 25-26, 36, 38, 48, 80-81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

The claims are drawn to a method for determining the gender of a canis familiaris subject comprising contacting a nucleic acid sample from the canis familiaris subject with a first and a second probe or primer which is complementary to consensus regions between SEQ ID NO: 22 and 23 and wherein such first and second probes or primers flank non-consensus regions between SEQ ID NO: 22 and 23 and binding to detect non-consensus regions to indicate the presence of X and Y chromosomal DNA of the species.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

Genbank Accession Number AB080686 (3/6/02) is directed to a canis familiaris amelx gene for amelogenin, partial cds from a Labrador retriever.

Tachi et al. (J. of Reproduction and Development, Vol. 48, No. 6, 2002) teaches a partial amelogenin (AMELX) from an extinct wolf species, *Canis lupus hodophilax* Temminck, a Japanese wolf. Tachi teaches an alignment from the domestic dog (*Canis familiaris*; Labrador retriever) which illustrates differences between the canine amelogenin sequences (see Figure 2 of Tachi). Tachi teaches that the results strongly indicate that polymorphisms of the nucleotide as well as the amino acid sequence might

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exist in this particular region of AMELX, depending upon the different breeds of domestic dogs, *Canis familiaris*. Tachi teaches that further molecular analysis of the intraspecific as well as the interspecific variations in the AMELX DNA will be needed to gain clear insight into the taxonomical and phylogenetic positions in the Japanese wolf.

Asano et al. (Am. Sc. J., Vol. 70, No. 10, pages J351-J362, October 1999) provides an alignment from wolf, dog, human, bovine, pig, mouse and rat amelogenin genes (Figure 6).

Guidance in the Specification and Working Examples

The specification specifically teaches that “additional regions of the canine amelogenin gene are likely to be identified from the complete canine amelogenin gene sequence that include nucleotide sequence differences between the copy of the gene on the X chromosome and on the Y chromosome (page 6, para 19). The specification also teaches that the sequences of the instant specification can be used to identify the nucleotide sequence of the entire canine (e.g. dog) amelogenin X chromosome gene and Y chromosome gene (page 25, para 81).

The specification teaches that “all canine DNA samples analyzed in this example, were dog DNA samples” (page 27). The specification further teaches DNA was isolated from various male and female dogs (page 28, para 93). The specification fails to teach the number, the species or the similarity between the females analyzed, for example.

The specification teaches that Figure 5 provides a comparison of consensus sequences of canine X (SEQ ID NO: 22) and Y (SEQ ID NO: 23) partial amelogenin sequences. The shaded sequences and gaps indicate differences between the canine AMELX and AMELY sequences.

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses an alignment of consensus sequences. The specification fails to provide whether each of the identified differences between the two consensus sequences is X or Y specific.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied

The claims are broadly drawn to detecting differences between the canine amelogenin gene on the Y chromosome and the canine amelogenin gene on the X chromosome.

The specification has not provided the skilled artisan any guidance to detecting differences between amelogenin gene on the Y and X chromosomes. As noted in the alignment provided by Tachi, the wolf and the dog partial DNA sequences of the amelogenin X gene have regions of variability. Tachi further teaches that the results strongly indicate that polymorphisms of the nucleotide as well as the amino acid sequence might exist in this particular region of AMELX, depending upon the different breeds of domestic dogs, *Canis familiaris*. Thus, it is unpredictable to the skilled artisan which regions of variability are conserved among the canine amelogenin gene over the genus and which regions are variability between amelogenin gene X and Y. Given the

teachings in the specification of a single consensus sequence within the *canis familiaris* species, it is undue and unpredictable which sequences are conserved over the entire genus to enable determining gender of the canine subject without further experimentation.

The specification teaches that Figure 5 provides a comparison of consensus sequences of canine X (SEQ ID NO: 22) and Y (SEQ ID NO: 23) partial amelogenin sequences. The shaded sequences and gaps indicate differences between the canine AMELX and AMELY sequences. It is unclear whether these shaded sequences are a difference between the consensus sequences of the X and Y chromosomes or whether the shaded sequences only are present in X chromosome or the Y chromosome. The difference being that an alignment showing differences between consensus sequences of the X and Y chromosome would not provide any information regarding whether the nucleotides/sequences present in the X, for example, are present at any frequency in the Y chromosome for example. If the consensus is the most likely nucleotide for the particular chromosome, this does not indicate that the alternative allele is not present and detection of the alternative allele would indicate a particular gender. If the shaded sequences are only present in X chromosome or Y chromosome, with statistical significance, then the ordinary artisan would be able to detect differences using this guidance. However, the specification fails to make clear or provide any information about the number of dogs (male and female) sampled, the specific breed/species sampled, analysis regarding whether alleles are present in the opposite chromosome, or even whether the allele present is merely an uninformative SNP. The art teaches that polymorphisms exist in nucleic acid sequences with frequency. In the event that only a single or a small number of highly related canines were sampled, the SNP may

exist in the consensus sequence which is not related to the gender determination of the canine subject.

Further it is unpredictable, as described above, whether detecting differences would be enabled for other breeds or species, since the art teaches such variability between the species. As Tachi teaches results strongly indicate that polymorphisms of the nucleotide as well as the amino acid sequence might exist in this particular region of AMELX, depending upon the different breeds of domestic dogs, *Canis familiaris*. Tachi teaches that further molecular analysis of the intraspecific as well as the interspecific variations in the AMELX DNA will be needed to gain clear insight into the taxonomical and phylogenetic positions in the Japanese wolf. Thus, detecting differences would not necessarily indicate gender differences, but may detect breed or species differences. Further, the art teaches that further experimentation would be required to practice the claimed invention as broadly as recited.

Each of these described issues would require much inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the specification fails to provide enough guidance or teachings to practice the scope of the claims as broadly as claimed. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized differences in sequences and

species, for example. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The response traverses the rejection. The response asserts the claims are supported because "one of skill in the art would predict that all breeds of dogs which fall under the typical dog would show substantially identical alignment for the amelogenin gene sequences as disclosed. This argument has been considered but is not convincing because the specification fails to provide clear guidance to the skilled artisan to determine gender. As provided in the rejection above, "the specification fails to make clear or provide any information or analysis regarding whether alleles are present in the opposite chromosome, or even whether the allele present is merely an uninformative SNP.

A consensus sequence is a way of representing the results of a multiple sequence alignment, where related sequences are compared to each other, and similar functional sequence motifs are found. The consensus sequence shows which residues are conserved (are always the same), and which residues are variable (see Wikipedia, last viewed June 21, 2006). Thus it is clear from the definition provided in the art that a consensus sequence is a compilation of canine sequences from multiple male dogs for SEQ ID NO: 23, for example. The compilation or consensus sequence would be a

sequence which considers all of the possible sequences of those in the population. A consensus sequence does not mean that SEQ ID NO: 23 is found in all males. The instant specification and the art do not provide any guidance as to which of the polymorphisms of SEQ ID NO: 23 are required to detect SEQ ID NO: 23. For example, in the event that a dog contained a C at position 52 of SEQ ID NO: 23, it is unclear whether this information is definitive of a female dog or whether the sequence of that male dog did not have the same sequence as the consensus sequence. It would seem that multiple regions would need to be analyzed to provide any reasonable certainty of success in determining the gender of the dog. The consensus sequence would not appear to be the sequence of any one individual but the pattern of all possible polymorphic regions.

The art teaches that polymorphisms exist in nucleic acid sequences with frequency. In the event that only a single or a small number of highly related canines were sampled, the SNP may exist in the consensus sequence which is not related to the gender determination of the canine subject." Also, the rejection above, states, "as Tachi teaches results strongly indicate that polymorphisms of the nucleotide as well as the amino acid sequence might exist in this particular region of AMELX, depending upon the different breeds of domestic dogs, *Canis familiaris*. Tachi teaches that further molecular analysis of the intraspecific as well as the interspecific variations in the AMELX DNA will be needed to gain clear insight into the taxonomical and phylogenetic positions in the Japanese wolf. Thus, detecting differences would not necessarily indicate gender differences, but may detect breed or species differences."

While the specification provides a "consensus" sequence for AMELX and a "consensus" sequence for AMELY. Neither the specification nor the art specifically provide any guidance to the skilled artisan how to use the claimed invention without

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further experimentation. The art suggests that the AMELX and AMELY genes are variable between species. Neither the specification nor the prior art suggest how the skilled artisan would determine whether differences are the result of natural variation between sequences or variations are related to gender differences. As discussed above, it is unclear what the consensus sequence represents. Unlike in many consensus sequences, the instant Figure 5 does not appear to show residues that are always conserved and which residues are variable with their variable sites.

The declaration filed on January 26, 2006 by Dr. Sue DeNise and Dr. Ferrie has been thoroughly reviewed. The declaration is directed to a specific primer pair which results in variable amplicon lengths depending on the gender of the individual. The instant claims are not commensurate in scope with the declaration. The MPEP provides that the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980). Here there is no evidence that the detection using the specific primers to obtain a 140 or 142bp amplicon indicates that any non-consensus region or any differences is indicative of gender discrimination.

Thus for the reasons above and those already of record, the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 1, 3-9, 12-13, 23, 25-26, 36, 38, 48, 80-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The claims are drawn to "a method for determining the gender of a canis familiars subject comprising contacting a nucleic acid sample from the canis familiaris subject with a first and a second probe or primer which is complementary to consensus regions between SEQ ID NO: 22 and 23 and wherein such first and second probes or primers flank non-consensus regions between SEQ ID NO: 22 and 23 and detecting non-consensus regions which are specific to SEQ ID NO: 22 and 23 and correlates with the presence of X and Y chromosomal DNA." It is unclear what defines a specific detection. The specification does not clearly provide any guidance what the metes and bounds of specific encompass. Further, detecting non-consensus regions which are specific to SEQ ID NO: 22 and 23 is unclear how the results would provide any information to whether the presence of X or Y was present. Clarification is request.

Conclusion

9. No claims allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.



J. Goldberg

Primary Examiner

June 21, 2006